Original Article

The Status of Insulin Access in Middle East-North Africa Region

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Abstract

Background and Objective: The current situation in the Middle East-North Africa (MENA) region makes it very difficult for many countries to have an effective policy to ensure the availability and affordability of different insulin types for many individuals with diabetes mellitus in any individual country. This article comprehensively reviews the possible barriers to insulin access in countries of this region and provides some solutions to mitigate these barriers. **Materials and Methods:** The framework for understanding the life-cycle of medicines of the World Health Organization (WHO) was adopted for this review with country-specific modifications. PubMed was used as an initial search builder using the country name and insulin as query terms in (title/abstract) for articles written in (English and French) which dealt with humans only between (2000–2022). Out of (578) published articles, only (42) articles were relevant and dealt with insulin access. Additional search through references of these articles and the websites of international health organizations added additional (32) references to have (79) references for the review. **Review (Results):** The countries in the MENA are lagging in the (Research, Development, and Innovation) and production of insulin and insulin delivery systems. There are some attempts by some countries to develop their national plan with the help of some big insulin manufacturers, with a suboptimal outcome. The local insulin production in some countries did not reach full national coverage. The difficult regional economic and political situations in many countries in the MENA imposed negatively on their citizens' insulin access, availability, affordability, cost, and insurance plans. **Conclusions:** There is a suboptimal level of insulin access for individuals with diabetes in the MENA countries, especially in the low-resourced countries. There is an urgent need to adopt country-specific healthcare policies to ensure uninterrupted insulin access and improved availability, with a lower affordable cost for individuals with diabetes from the public and private sectors.

Keywords: Diabetes, healthcare, insulin, middle east, north africa

Introduction

A century after the great innovation of insulin, insulin availability remained a challenge in different parts of the globe, especially in the countries of the Middle East-North Africa (MENA) region.[1]

Information about insulin access, availability, affordability, and pricing in the MENA was discussed by many studies as a part of global regions, with no consideration of the unique challenges in this area on these factors.[2]

There is a complex interplay between the lack of governmental policies regarding insulin affordability and availability and the patient's out-of-pocket costs to cover the continuous need for insulin.[1] Globally, the private sector had the upper hand,

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with minor contributions from international governmental policies, International Diabetes Federation (IDF), and the World Health Organization (WHO).[3]

In addition to these globalized problems, the highest region with diabetes worldwide, MENA, possessed an unprecedented scale of emergencies, mainly due to political conflicts in several countries. Accordingly, more than 62 million people across MENA seem to require healthcare due to the proposed shortages in health staff, medicines, and medical supplies.[4]

Individuals with diabetes, and particularly those with type 1 diabetes mellitus (T1DM), are particularly vulnerable in humanitarian crises, given disrupted health services, lack of essential medications and supplies like insulin and blood glucose test strips, loss of medical records, lack of disease awareness between patients and healthcare workers (HCW), and impeded food supplies due to insecurity and population movement.[5-7]

There are enormous challenges and barriers to insulin access. This article comprehensively reviews the possible barriers to optimal insulin access in the countries of MENA.

Materials and Methods

To understand the complexity of the possible barriers to insulin access in this region, we adopted the WHO's framework on understanding the life-cycle of medicines[8] to provide a platform for our review, with different country-specific modifications.

To get comprehensive information and data about insulin access status in the MENA region, a thorough search was done through the published articles in PubMed.

We used the country name (Afghanistan, Pakistan, Iran, Iraq, Syria, Lebanon, Palestine, Jordan, Saudi Arabia, Kuwait, Bahrain, Qatar, United Arab Emirates, Oman, Yemen, Egypt, Sudan, Libya, Tunisia, Algeria, Morocco, Middle East, and North Africa), and (insulin) as query indicators for the search in (title/abstract) for articles written in (English and French) which dealt with human only, between (2000–2022).

We get a net result of (945) published articles. Removal of the duplicate titles resulted in (578) articles. Articles that were relevant to the logistic insulin access and policies in the MENA countries were 42 articles only. An additional thorough search on the (1920) references of these (42) articles added additional (32) references, which included published articles, international aid organizations reports, press reports, and other official trustful sites. The final number of used references in this review included (79) references.

Results

The regional and country-specific situations were considered during this review, which adopted the general platform of the life-cycle of medicines by the WHO, which is not specific to insulin.

Research and development (R&D) and innovation

Kaplan and Beall examined insulin-related patent threads to assess this step, but they did not find any active patent for human insulin. Many patents for analog insulins expired in 2015 for products already on the market, i.e., the market dominance of analogs was not an intellectual property exclusivity function.[9,10]

Most of the patents were filed by large multinational manufacturers, with a few of the patents identified being from companies in India and China. In the United States, 53% of patents were for insulin delivery devices rather than insulin itself.[11] For the MENA, Morocco, Algeria, Egypt, Sudan, Israel/Palestine, and Lebanon filed a few insulin-related patents after 1995.[10,12] Global mapping of the insulin patent estates may encourage many manufacturers to open multiple regional and far smaller markets.[10]

After 2005, Iranians created a complex multidisciplinary interactive, innovative biotechnology network to guide the innovative drug development process, which did not include insulin alone, but all medications in progress. One of these achievements is the Eastern Mediterranean Health Genomics and Biotechnology Network and Regional Network in 2005, which was established to bring the scientists of this region together. More than eight countries are members of this network, including Saudi Arabia, Egypt, Pakistan, Oman, Bahrain, Iran, Morocco, Tunisia, and Syria.[13]

Even in the presence of adequate human resources and the scientific communities willing to participate, the main limitation in the R&D of any medicine is the funding. Another problem is the poor collaboration among academic groups and industrial centers on projects.[14]

The country-specific rewards to risks index (RRI) guided and often limited the intents of many big pharmaceutical firms to open innovative lines in MENA. Fitch Solution provided these RRIs, which were not promising even for the MENA high-income countries (HIC). The current RRI make many firms reluctant to start innovative pharmaceutical work in MENA. The 2019 RRIs of the MENA were: United Arab Emirates (UAE) (65.6), Kingdom of Saudi Arabia (KSA) (59.4), Kuwait (53.0), Qatar (50.7), Lebanon (48.6), Morocco (48.4), Algeria (47.6), Jordan (47.2), Bahrain (46.5), Oman (45.6), Egypt (38.6), Iran (37.9), Tunisia (36.5), Iraq (35.4). The global average is (50.0), while the regional average is (47.2).[15]

Manufacturing

Insulin is a complex biological product that requires specific expertise to manufacture to ensure a high-quality, safe, and efficacious product. Eli Lilly, Novo Nordisk, and Sanofi Aventis have a 96% share of the insulin market by

volume and hold 99% of the market by value. There were minor contributions from 42 other international insulin manufacturers in 17 countries.[1,9,16,17]

The Largest company in the MENA is Julphar (headquarters in UAE), which provides 0.25% of the globally registered insulin products, the seventh top global insulin manufacturer. UAE infrastructure helps create better insulin accessibility programs and ensures diversity for Julphar.[17]

Egypt, the low, middle-income country (LMIC), had about 2% of the world population with diabetes, had three local insulin manufacturers, in addition to the big three global insulin manufacturers (Novo Nordisk, Sanofi, and Eli Lilly), and often supplied countries with high demand.[18]

Tables 1 and 2 showed a list of insulin manufacturers with products registered and/or sold by country. Egypt and Iran had diverse insulin supplies from the big three companies and local registered manufacturers. Julphar provided comprehensive coverage for countries in the MENA.[17]

The country-wise experience of insulin manufacturing is different. Patients may denounce the quality of homemade medical products. They considered these insulin types ineffective or had significant side effects.[19]

For Iran, the harsh effect of economic sanctions was evident even in insulin manufacturing within the country. Till December 2020, Iran had two domestic insulin lines: Basalin, a product by Iran-based biopharmaceutical company Pooyesh Darou, and insulin from Novo Nordisk Pars, a subsidiary of Novo Nordisk in Alborz Province. According to Pooyesh Darou officials, the Iranian Basalin is a transfer of technology from a Chinese company bought by Sandoz. Novo Nordisk's first insulin production line began in August 2020. Still, the availability is questionable.[20]

In KSA, AJA Pharma (part of Saudi Chemical Company Holding SCCH) and Eli Lilly Saudi Arabia signed an agreement in September 2020 to locally produce insulin within KSA and improve strategic cooperation through biomedical capabilities. This step will ensure drug security in KSA, train national personnel through a well-designed

Table 1: Insulin manufacturers with products registered and/or sold by different countries in the MENA region[17]

Country	Big Three Manufacturers	Additional Manufacturers
Algeria	Novo Nordisk, Sanofi, Eli Lilly	Julphar
Bahrain	Novo Nordisk, Sanofi, Eli Lilly	
Egypt	Novo Nordisk, Sanofi, Eli Lilly	Amoun Pharmaceuticals, SEDICO, VACSERA
Iran	Novo Nordisk, Sanofi	Bioton, Exir, Wockhardt
Jordan	Novo Nordisk, Sanofi, Eli Lilly	Bioton, Julphar
Kuwait	Novo Nordisk, Sanofi, Eli Lilly	
Lebanon	Novo Nordisk, Sanofi, Eli Lilly	Julphar
Morocco	Novo Nordisk, Sanofi, Eli Lilly	
Oman	Novo Nordisk, Sanofi, Eli Lilly	Julphar
Pakistan	Novo Nordisk, Sanofi, Eli Lilly	Biocon, Bioton
Qatar	Novo Nordisk, Sanofi, Eli Lilly	Julphar
Saudi Arabia	Novo Nordisk, Sanofi, Eli Lilly	Julphar
Sudan	Novo Nordisk, Sanofi, Eli Lilly	
Tunisia	Novo Nordisk, Sanofi	Julphar
United Arab Emirates	Novo Nordisk, Sanofi, Eli Lilly	Biocon, Julphar, SEDICO

Adapted from ACCISS Study. Insulin Market Study, April 2016.
https://haiweb.org/wp-content/uploads/2016/04/ACCISS_Insulin-Market-Profile_FINAL.pdf.

Table 2: List of independent insulin manufacturers in the MENA region[17]

Company Name	Headquarters Country	Number of Countries with Products Registered and/or Sold	Percent of Countries with Products Registered and/or Sold
Julphar	UAE	13	10.74%
SEDICO	Egypt	2	1.65%
VACSERA	Egypt	1	0.83%
Amoun Pharmaceuticals	Egypt	1	0.83%
Exir	Iran	1	0.83%

Adapted from ACCISS Study. Insulin Market Study, April 2016
https://haiweb.org/wp-content/uploads/2016/04/ACCISS_Insulin-Market-Profile_FINAL.pdf

competency program, and create more qualitative employment opportunities in line with the KSA's Vision 2030.[21]

For Tunisia, successful attempts to manufacture insulin in Tunisia were promoted by KAN Pharma (Swassi, Mahdia District). Still, the production was intended for export.[22]

The Egyptian experience is a success story. Late in 2002, the Egyptian authorities faced an acute insulin shortage. In cooperation with European and Chinese international partnerships, the Vaccine and Inoculation Authority (VACSERA) gained permission to manufacture recombinant human insulin. Local VACSERA production has saved considerable governmental payments and partially freed the national insulin availability from long-standing foreign monopoly.[14]

Algeria could be able to manufacture insulin locally after 2022 through a strategic partnership between state-owned SAIDAL Group (Groupe Saidal) and Novo Nordisk. SAIDAL Group is building a novel production facility in Constantine. The facility used high-quality raw materials supplied by Novo Nordisk to produce modern insulin.[23,24]

The minor contribution of the local insulin manufacturers can be seen in Table 3. However, they contributed a minimal share of insulin export to different parts of MENA and outside MENA. Of the countries identified as local insulin producers, Iran did not export any insulin from 2004–to 2014.[18]

The dominance of the big three insulin produces an additional barrier to insulin access, and those old products have been replaced with newer ones. Still, no manufacturers of generic biosimilar products have emerged effectively on the market.[16,17,26]

Challenges in introducing generic or biosimilar insulins (Biohackers)

Incentivization of potential generic manufacturers toward new national insulin markets and off-patent products can be achievable.[10]

Generic or biosimilar insulin production is more complex, especially from an internationally agreed regulation perspective.[27] The ongoing manufacturing process could affect the equivalence of the end molecule to the original protein, generating interchangeability issues that further complicate the uptake of biosimilars.[28,29]

Although innovations in insulin types might be unnecessary, improvements in different health system factors for diabetes drug delivery and care are necessary.[9]

Kessel[30] argues that the pharmaceutical industry's roles comprise improving health and generating profits for shareholders. Increasingly, a shift has focused more on profits and less on patient care and outcomes.

Co-production in low- and middle-income countries (LMIC) requires recognition from researchers, funders, and stakeholders. These parties must work together from the beginning of the research process. However, this may raise an ethical issue of power relation inequality between different parties based on their knowledge and values.[31,32]

Marketing registration

Registering the insulin types nationally is a vital step before marketing authorization. It requires scientific evaluation of insulin to ensure that it fulfills specific safety, efficacy, and quality standards. Registering biosimilar generic insulin demands additional steps by including clinical trials to ensure safety and efficacy. These requirements affect the cost and biosimilar marketing profile.[1]

Many regulatory agencies in the LMIC lack the technical capacity to evaluate the data on different types of insulin, which adds additional barriers to insulin access in the area. This urged WHO to launch its prequalification program to allow any insulin producer to submit their product for regulatory review by WHO.[33] Through strengthening regulatory harmonization by adding local products to the WHO prequalification program, competition in the insulin market will hopefully be increased while ensuring the stability of the affordability, safety, and efficacy of local products for different countries with lower prices.[1,16,33,34]

Regarding product registrations, 88.7% of (global) insulin registrations are for products from the three multinational companies [Table 4].[17]

Table 3: Total (kg) of insulin exports from Egypt and UAE compared to Germany[25]

Country	Total quantity of retail insulin exported from country from 2000–2013, kg	Total quantity exported from country in comparison to Germany, %	Number of countries/territories to which insulin exported	Number of WHO regions to which insulin exported
Egypt	32218	0.3	10	2 (AFRO and EMRO)
United Arab Emirates	114050	0.9	6	4 (AFRO, EMRO, EURO, and SEARO)
Germany	12899410	100	121	6

Adapted from Beran D *et al*. Diabet Med. 2019 Jun;36(6):726–33

Abbreviations: AFRO, WHO Regional Office for Africa; EMRO, WHO Regional Office for the Eastern Mediterranean; EURO, WHO Regional Office for Europe; SEARO, WHO Regional Office for Southeast Asia

To date, regulations of biosimilars are not standardized and continue evolving.[35] The governments are responsible for introducing novel and highly cost-effective products in healthcare for their populations.[3]

A- Selection

The WHO's Model Essential Medicines List (EML) provides soluble and intermediate-acting insulin vial forms.[37] 2019 WHO EML did not include the long-acting insulin analog because of the insufficient evidence about the efficacy and cost-effectiveness of insulin analogs over human insulin.[38,39]

MENA countries developed their NEML far before the recent WHO EML and included many insulin analogs. Libya developed the NEML (2005), Pakistan (2007), Syria and Tunisia (2008), Bahrain, Oman, UAE, and Yemen (2009), Iraq (2010), Jordan (2011), Palestine, Morocco, Egypt, and KSA (2012), Iran (2013), and Afghanistan, Sudan, and Lebanon (2014).[17,40]

Table 5 describes the countries listing specific rapid and/or long-acting analog insulin as part of their NEML. Saudi Arabia lists three types of rapid-acting analog insulin. Algeria, Jordan, KSA, and Tunisia listed the highest number of long-acting analog insulin types in each country ($n = 2$).

Table 6 shows mean patient prices for three insulin analogs in some MENA regions' private and healthcare sectors. The prices were approximately similar in the private sector for different types with minor differences in the MENA.

There is an extensive variation in glargine prices in the public and private sectors. Glargine ranged from $16.60 in Vietnam to $109.67 in China. Wide price variations across countries were also seen in the private sector, e.g., glargine was $8.32 in India and $196.46 in Venezuela.[41]

In general, the increased competition from generics lowers the prices, with unclear effects on its affordability.[3,42]

Personal preference must be considered for future research. A study from Jordan showed that although the vials cost less direct per patient than cartridges, there was a substantial wastage reduction.[43]

A study from Iran revealed that the intermediate-acting insulins such as NPH, regular, and aspart insulins were affordable, while none of the long-acting insulins were affordable.[44] Another study confirmed the constant affordability of regular and intermediate-acting insulin, and the premixed insulin became affordable only in the last three years of their study (2010–2012). Novel insulin preparations such as premixed aspart insulin and a combination of aspart and glargine were constantly non-affordable during the study period (2000–2012). In 2012,

Table 4: Total registered insulin products by region and per country[17]

Country	Income level	No. of human insulin products	No. of analog insulin products	No. of animal products	Unknown	Total
Egypt	UMI	54	13	1	3	71
Morocco	LMI	19	22	1	0	32
Saudi Arabia	HI	16	22	1	0	39
Sudan	LMI	12	1	0	0	13
Lebanon	UMI	11	0	0	0	11
Oman	HI	9	23	0	0	32
Algeria[1]	UMI	3	1	0	0	4

Adapted from ACCISS Study. Insulin Market Study, April 2016.
https://haiweb.org/wp-content/uploads/2016/04/ACCISS_Insulin-Market-Profile_FINAL.pdf
Abbreviations: HI, high income; LMI, lower middle income; UMI, upper middle income
[1] Algeria had one of the most demanding registration systems in the MENA region[36]

Table 5: Analogue insulin availability in NEML in some MENA countries[17]

Country	Analogue Insulin Rapid-Acting			Analogue Insulin Long-Acting	
	Glulisine	Aspart	Lispro	Detemir	Glargine
Algeria	0	1	1	0	2
Bahrain	0	0	0	0	1
Iran	1	0	0	0	1
Iraq	0	0	1	0	0
Jordan	0	1	0	1	1
Oman	0	0	1	0	1
Saudi Arabia	1	1	1	1	1
Tunisia	1	0	0	1	1

Adapted from ACCISS Study. Insulin Market Study, April 2016.
https://haiweb.org/wp-content/uploads/2016/04/ACCISS_Insulin-Market-Profile_FINAL.pdf

the cost of the combination therapy with aspart and glargine insulin was one day higher than the premixed aspart insulin in accordance with the least daily wages (LDW) (5.8 to 4.8 of the LDW).[45] Moreover, the insulins' affordability further improved due to the memorandum of understanding of the health ministry with health insurance organizations.[44]

It revealed that oral mono, dual and triple medication therapies might be affordable for Iranian patients with the lowest wages. In contrast, insulin therapies may represent significant barriers to treatment in combination and at increased doses – despite their good health insurance coverages.[44]

B- Pricing

The mean patient prices of analogs are more than three to ten folds the human insulin cost, as shown in Tables 7 and 8. These prices might be affordable for individuals from HIC, but not LMIC, like the present comparison between KSA and Sudan according to the LDW in Table 9. The reimbursement and procurement prices are discussed individually.[41]

The final price is also linked to comparative insulin availability in public and private healthcare sectors, with more prices for the latter.[46] The regulation prices are regulated centrally. For example, Drug prices are determined by the Iranian Food and Drug Administration (IFDA) Pricing Commission. Decisions on the final fixed drug prices consider the balance between production and import expenses.[47]

The diabetic population in KSA has widely accepted the presence of branded and imported drugs in the country driven by socioeconomic parameters, leading to the accelerating growth of the branded diabetes drugs market in the country. In addition to branded products, the drug market included many national manufacturers and suppliers involved in the R&D and supply of diabetes-related drugs.[48]

Table 6: Mean patient price in USD, for aspart, glargine, and lispro in some MENA countries' public and private sectors.[41] Comparative data for China, Vietnam, India, and Venezuela are listed for comparison

Country	Mean patient price USD 10 ml 100 IU analog insulin					
	Public Sector			Private Sector		
	Aspart	Glargine	Lispro	Aspart	Glargine	Lispro
Bahrain				37.23	54.63	31.18
Saudi Arabia				31.78	55.81	
United Arab Emirates				39.33	69.48	39.37
Iran	39.70	40.87		39.70	40.87	
Jordan				32.21	56.95	34.60
Lebanon					55.29	35.37
China	50.40	112.93	46.37	49.96	109.67	
Vietnam		16.60			9.62	
Venezuela				116.06	196.46	95.01
India				16.36	8.32	10.59

Adapted from ACCISS Study. Insulin Price Profile, April 2016.
https://haiweb.org/wp-content/uploads/2016/04/ACCISS-Prices-report_FINAL-1.pdf

Table 7: Mean patient prices, USD, for isophane, regular and regular/isophane 30/70, public and private sector, in some MENA countries[41]

Country	Mean patient price, USD, 10ml 100IU human insulins					
	Public Sector			Private Sector		
	Isophane	Regular	Regular/Isophane 30/70	Isophane	Regular	Regular/Isophane 30/70
Saudi Arabia				16.65	16.65	16.65
United Arab Emirates				17.19	19.34	16.89
Iran	4.20	4.20	4.20	4.20	4.20	4.20
Jordan				15.70	15.21	13.44
Lebanon				15.70	15.21	13.44
Egypt				4.06	3.59	4.06
Pakistan				5.50	5.50	4.75
Sudan	8.78	8.78	8.12	11.66	12.04	13.75

Adapted from ACCISS Study. Insulin Price Profile, April 2016.
https://haiweb.org/wp-content/uploads/2016/04/ACCISS-Prices-report_FINAL-1.pdf

Table 8: Mean patient price, USD, for aspart, glargine, and lispro, in public and private sectors in some MENA countries[41]

Country	Mean patient price USD 10ml 100IU analog insulins					
	Public Sector			Private Sector		
	Aspart	Glargine	Lispro	Aspart	Glargine	Lispro
Bahrain				37.23	54.63	31.18
Saudi Arabia				31.78	55.81	29.51
United Arab Emirates				39.33	69.48	39.37
Iran	39.70	40.87		39.70	40.87	
Jordan				32.21	56.95	34.60
Lebanon					55.29	35.37
Sudan		45.03			59.04	

Adapted from ACCISS Study. Insulin Price Profile, April 2016
https://haiweb.org/wp-content/uploads/2016/04/ACCISS-Prices-report_FINAL-1.pdf

Table 9: Mean affordability of selected human and analog insulins in Saudi Arabia and Sudan[41]

Insulin Types		No. of days' wages to buy 10ml 100IU human insulin, private sector	
		Saudi Arabia	Sudan
Human Insulins	Isophane	0.6	4.9
	Regular	0.6	5.1
	Regular/Isophane	0.8	5.3
Analogue Insulins	Aspart	1.2	
	Aspart/Prot.	1.2	
	Degludec		
	Detemir	2.2	
	Glargine	2.1	25.00
	Glulisine	1.1	
	Lispro	1.1	
	Lispro/Prot.	1.2	

UAE, United Arab Emirates
Adapted from ACCISS Study. Insulin Price Profile, April 2016
https://haiweb.org/wp-content/uploads/2016/04/ACCISS-Prices-report_FINAL-1.pdf

Novo Nordisk adopted a differential pricing policy in the three least developed countries (LDC) from the MENA (Afghanistan, Sudan, and Yemen). The differential pricing policy is part of the global initiatives to promote access to healthcare for all LDCs, and to offer human insulin in vials to all LDCs at or below a market price of 20% of the average prices for human insulin in vials in the western world.[49]

The burden of diabetes and its complications for Iranians with diabetes is complex due to their struggle with international sanctions. Due to shortages or exorbitant prices, they have long grappled with insulin shortages, test strips, glucometers, syringes, and insulin pumps due to the harsh sanctions.[50] Sanctions on Iran made many insulin-producing firms reluctant to import their products to Iran due to fear of their future finances. However, the drugs were excepted from the sanctions. That behavior urged Iran to pay Novo Nordisk to double the price offered to other countries and more than five times its production cost for specific shipments of insulin pens, although Novo Nordisk denies insulin price gouging. Consequently, the consumer price will be high and non-affordable.[51]

C-Reimbursement [Table 10]

Some governments compensate patients with diabetes for their out-of-pocket costs equal to what was spent. Morocco and UAE were the only MENA countries that developed successful health policies regarding reimbursement of different insulin types. However, the income levels differed, i.e., Morocco, the LMIC, and UAE, the HIC. UAE reimburses 21 types of insulin compared to 17 types by Morocco. Analog insulin (Detemir and Glargine) in both countries had the highest reimbursement prices compared to the minimal reimbursement cost of regular rapid-acting insulin.[1,41]

A meta-analysis of the economic cost of T2DM in the EMRO showed that the annual treatment costs of diabetes were variable between countries in EMRO. The highest cost belongs to Qatar, and the lowest is for Iran.[52]

Procurement and supply

Local governmental pricing policies and approaches will affect how medicines are procured. In most LMICs, insulin is purchased via centralized tenders for the public sector.[53]

Table 10: Reimbursement prices by brand in UAE and Morocco[41]

Insulin Type	Brand	Country	Price USD	N
Human Insulin				
Isophane	Biosulin N®	Morocco	12.10	1
	Humulin N®	Morocco	22.19	2
		UAE	10.29	1
	Insulatard®	Morocco	18.83	3
		UAE	12.66	2
	Insulet N®	Morocco	7.91	1
	Insulin Bio NPH®	UAE	6.96	1
	Jusline N®	UAE	8.58	1
Lente	Monotard®	UAE	11.72	1
Regular	Actrapid®	Morocco	18.83	3
		UAE	13.44	3
	Biosulin R®	Morocco	12.10	3
	Humulin R®	Morocco	12.10	1
		UAE	10.29	1
	Insulet Rapid®	Morocco	7.91	1
	Insulin Bio R®	UAE	6.96	1
	Jusline R®	UAE	8.58	1
Regular/Isophane 30/70	Humulin 30®	Morocco	22.19	2
		UAE	10.29	1
	Insulet Mix 30®	Morocco	7.91	1
	Insulin Mix 30/70®	UAE	6.91	1
	Jusline 30®	UAE	8.58	1
	Mixtard 30®	Morocco	18.83	3
		UAE	15.54	4
Insulin Analogue				
Aspart	NovoRapid®	UAE	31.64	2
Aspart/Protamine 30/70	NovoMix 30®	Morocco	34.48	2
		UAE	32.75	2
Detemir	Levemir®	Morocco	56.26	2
		UAE	46.76	2
Glargine	Lantus®	Morocco	47.35	7
		UAE	48.65	4
Glulisine	Apidra®	Morocco	14.18	5
		UAE	26.57	3
Lispro	Humalog®	Morocco	32.71	2
		UAE	27.57	3
Lispro/Protamine 25/75	Humalog Mix 25®	Morocco	32.99	2
		UAE	27.57	3
Lispro/Protamine 50/50	Humalog Mix 50®	UAE	27.96	1

Abbreviations: UAE, United Arab Emirates

Adapted from ACCISS Study. Insulin Price Profile, April 2016

https://haiweb.org/wp-content/uploads/2016/04/ACCISS-Prices-report_FINAL-1.pdf

Dependent on the healthcare sector and the national health policies, the price mark-ups difference between the procurement and patient prices might upsurge according to import tariffs, the costs of (storage, transportation, and dispensing), and sales taxes.[1] These mark-ups may reach (8.7–47.7%) of selling prices for locally produced insulin and (10%-565.8%) for imported insulins.[54]

Many countries lack adequate infrastructure for procurement, insulin supply chain, and insulin distribution, resulting in low availability and lower healthcare levels.[9]

The reimbursement prices [Table 10] are far higher than government procurement prices [Table 11] for human and analog insulins. This indicates that national insurance policies may not use their great potential to leverage lower prices. Insurance systems mustn't shift costs to people on insulin.[1,41] The data in Table 11 regarding Iran are sustained until the imposition of the harsh 2019 sanctions, which changed the procurement profiles in the Iranian pharmaceutical markets, as stated by the Iranian FDA officials, by being significantly foreign

Table 11: Procurement prices, USD for 10ml 100IU insulin, in some MENA countries, according to brand and presentation[17]

Brand	Manufacturer	Presentation	Country	Mean Procurement Price USD
Human insulins				
Actrapid®	Novo Nordisk	Cartridge	Jordan	9.14
		Pen	GCC	8.33
		Vial	GCC	2.82
			Pakistan	2.42
			Sudan	3.34
Biosulin N®	Kharazmi	Vial	Iran	4.36
Biosulin R®	Kharazmi	Vial	Iran	4.36
Insuget 30/70®	Getz	Vial	Pakistan	2.06
Insuget R®	Getz	Vial	Pakistan	2.06
Insulatard®	Novo Nordisk	Vial	GCC	2.82
			Sudan	3.34
Jusline R®	Julphar	Vial	Afghanistan	4.46
Lansulin 30/70®	Exir	Vial	Iran	4.36
Lansulin N®	Exir	Vial	Iran	4.36
Lansulin R®	Exir	Vial	Iran	4.36
Mixtard 30/70®	Novo Nordisk	Vial	GCC	2.82
			Pakistan	2.42
			Sudan	3.34
			UNRWA	2.92
Novolin N®	Novo Nordisk	Vial	UNRWA	2.92
Novolin R®	Novo Nordisk	Vial	UNRWA	2.92
Vitasulin N®	Vitane	Vial	Iran	4.36
Vitasulin R®	Vitane	Vial	Iran	4.36
Analog insulins				
Apidra®	Sanofi	Pen	GCC	20.67
Humalog®	Eli Lilly	Pen	GCC	24.53
		Vial	GCC	14.14
Humalog Mix 25®	Eli Lilly	Cartridge	GCC	24.53
		Pen	GCC	24.53
Humalog Mix 50®	Eli Lilly	Cartridge	GCC	22.50
Lantus®	Sanofi	Pen	GCC	42.03
			Iran	36.89
		Vial	GCC	36.80
Levemir®	Novo Nordisk	Pen	GCC	41.00
		Vial	GCC	34.00
NovoMix 30/70®	Novo Nordisk	Pen	GCC	24.77
			Iran	34.20
NovoRapid®	Novo Nordisk	Pen	GCC	24.77
			Iran	34.20
		Vial	GCC	13.95

Adapted from ACCISS Study. Insulin Market Study, April 2016
https://haiweb.org/wp-content/uploads/2016/04/ACCISS_Insulin-Market-Profile_FINAL.pdf
Abbreviations: GCC, Gulf Cooperation Council; UNRWA, United Nations Relief and Works Agency for Palestine Refugees

currency-intensive and made harder during the difficult time of sanctions.[17,55]

Prescribing

Insulin prescribing is affected by the type and place of diabetes care settings, whether primary, secondary, or tertiary. In some settings, only specialists can prescribe insulin. There is a discrepancy in experience, expertise, and knowledge at the hospital and PHC levels.

Whether the healthcare professionals were trained to use human or analog insulins or both and whether any drug manufacturer might have on doctors' prescribing decisions were another issue in prescribing insulin.[1] There are different MENA experiences:

VISION study[56]

The study unveils the issue of clinical inertia in countries of the MENA region in diabetes management and

the importance of early insulin initiation and timely intensification. The high HbA1c levels support this conclusion at the time of insulin initiation. A few patients achieved HbA1c of even <7.5% despite insulin treatment and intensification over the 18 months study period. However, an increase in satisfaction with diabetes therapy and QoL measures indicates that the patients are satisfied with their insulin therapy. The finding is that most Egyptians with diabetes were initiated on premixed insulin and were using the free sulfonylureas offered by the government insurance system. In contrast, other drugs and basal insulin analogs are relatively expensive.

In greater Tunis

A study showed that healthcare centers in which a regional diabetes coordinator doctor with a particular interest in diabetes worked were found to have a significantly higher care recording for diabetic patients.[57]

Family physicians

A survey involving 292 family physicians from 15 MENA countries showed that insulin benefits outweigh its risks and that patient education and training are keys to successful insulin initiation. However, the majority did not believe that most patients with T2DM will eventually need to go on insulin therapy. Around one-third of the family physicians in the study usually refer their patients with T2DM to endocrinologists for insulin initiation, which constitutes a significant primary care practice gap.[58]

MOSAIc Study[59]

The data in MOSAIc Study highlight the complex interplay of demographic, medical, and self-reported data with health status and T2DM treatment regimens and underscore the limitations of a one-size-fits-all approach to improving the management of T2DM, improving insulin adherence, and optimizing the clinical outcomes.

Abu Dhabi experience

In 2018, Abu Dhabi (UAE) authorized generic prescribing as the first choice of dispensing to keep costs down. If the patient prefers the higher-priced innovator brand, they can buy it after forfeiting the price difference between the innovator and the lowest generic prices. This model was previously applied in Finland, Denmark, and Sweden.[60]

Dispensing

Dispensing is the insulin provision by the healthcare system to an individual. Insulin dispensing is a challenge in many LMICs. The geographical burden with the considerable distance between communities and healthcare facilities may result in a financial barrier that may affect the service delivery, as people with diabetes spend a large share of their income on their care.[1,46] Another barrier in dispensing is the selective availability and healthcare coverage between primary, secondary, and tertiary healthcare facilities regarding insulin which ranges from 17.4 to 100% in public sectors (median: 42.9%). Also, there is a logistic problem with the possible shortage of insulin provision to the public health pharmacies, i.e., insulin is unavailable when the individual gets it.[1,9,16]

The socioeconomic circumstances compound these system-level barriers. Populations from the rural, urban poor, marginalized, indigenous, and those with lower levels of education have access to health services and may underutilize the available services.[46]

Insulin affordability depends on many factors, including the insulin types purchased, the additive price mark-ups, and the availability of insulin in the public sector.[9]

Insulin, among other medications in the Iranian healthcare system, is primarily distributed by six government-owned companies, with about 20 currently active. Overall, the ten largest distributors have a 75% market share, showing a high level of consolidation, which makes leveraging existing local networks an attractive option.[47]

The topographic access to health facilities may be a problem for dispensing and using insulin in some MENA areas. The first example is how the native Kashmiris could not have enough care and insulin access due to the impedance of the agro-climatic condition. Ultimately, many patients rationed and/or delayed their dosing as a desperate strategy to cope with the shortage.[61] The second example is the problem of internally displaced individuals due to the Iraqi and Libyan conflicts, which exerts extra pressure on their inadequate healthcare infrastructure.[62] The third example is how the Syrian conflict affected the dispensing of the minimal amount of insulin according to the current political and geographical barriers to the areas under relative governmental control due to security reasons. Aid organizations like WHO, IDF, ICRC, Life for a Child, DirectRelief, and T1International work to provide insulin for Syrian refugees.[63,64] Individuals under these circumstances give less prioritization to healthcare.

Insulin use

The high insulin costs urge some individuals to forego or economize their insulin injection regimen by omitting some doses. Initiation and continuation of any insulin type are influenced by the patient's socioeconomic status and knowledge about diabetes.[1,65]

Some Insulin analogs were listed in many NEMLs, although their affordability and availability in the public healthcare sector were questionable.[17] Also, their cost-effectiveness studies in MENA were variable towards or against their use.

In a large cross-sectional study from Iran, which involved 19,503 participants, Ebrahimi and her colleagues recommended against the use of higher costing insulin pens compared to traditional vials and syringes. Insulin pen was not associated with improved glycemic control

and lipid profile in their sample.[66] A small sample study (n = 74) in Lebanon showed the opposite opinion. The study recommended using the insulin pen as it was significantly more straightforward and less painful than the conventional vial/syringe.[67]

Hyassat and her colleagues from Jordan recommended the use of premixed human insulin (BHI30) to achieve better HbA1C reduction compared to premixed insulin analog (BIAsp30), with less cost ($31 per month and $75 per month for BHI30 and BIAsp30) respectively. However, it caused more weight gain and mild hypoglycemia.[68]

On the other hand, in a study involving four countries from the Near East (Lebanon, Jordan, Israel, and Pakistan), the authors recommended using insulin Detemir to improve glycemic control without increasing the risk of hypoglycemia or weight gain.[69] Yet, their study was observational and lacked the control arm.

Most Afghanis with diabetes lack such luxury. Many Afghani people with diabetes could not adjust their insulin dose correctly or not at all according to the regular measurements of glucose due to the costly diabetes care, which may reach up to $110.[70]

Additional burdens beyond insulin

The accessibility of insulin syringes, delivery systems, and glucose measurement tools is questionable and poor in many LMICs.[71-74]

The disposable insulin delivery pen represented a challenge for many patients, and its availability was always questionable. Julphar had an agreement to use the BD Vystra™ disposable pen for its insulin products in UAE.[75] Also, Julphar has signed an exclusive distribution agreement with Valeritas Holdings Corporation, the medical technology company, to provide its V-Go® Wearable Insulin Delivery device to the GCC. Julphar will have the right to market promotion and sales to diabetes clinics and patients in the GCC.[76]

Other barriers to optimize diabetes care are present, such as lack of HCW training and shifting specific diabetes treatment roles from doctors to nurses and other healthcare professionals. Logistically speaking, the poorly-adapted healthcare system, policies, and funding in many LMICs failed to adapt to the culturally-specific needs of individuals with diabetes, excreted additional challenges.[77]

The cold chain for insulin production is not a challenge at the production or health system levels but could be a problem at the individual's home.[9]

Several factors can affect the continuous supply and affordability of goods, such as interruption of supply due to, for example, military turmoil, sanctions, disrupted supply chain, the monopoly of a foreign supplier, and technical, human, and natural risks.[78]

Conclusions

In conclusion, insulin access in many MENA countries is suboptimal, especially in middle- and low-income countries. There are different levels of insulin access in the MENA countries, depending on the individual country's political, economic, and geographical status, healthcare policy and budget, healthcare infrastructure design, insurance system, and public-private sectors healthcare services coverage. Still, many country-specific challenges in the MENA make insulin access a dilemma.

Recommendations

Given the current relative crisis in many MENA countries, it is prudent to recommend some practical steps to ensure better insulin access to people with diabetes in different healthcare levels and health sectors.

It is challenging to ensure implementation of the following recommendations on the regional or international levels because of the non-uniformity of the MENA countries, i.e., the MENA contains countries with the highest and the lowest income countries in the world and some countries in between.

At the country level, developing a country-specific healthcare policy that ensures continuous and diverse insulin access, including insulin delivery tools to patients in different areas of the country, is mandatory. This policy must ensure a timeline to rectify the inherited weakness at the PHC level, which is evident in many MENA countries. Strengthening the PHC will lessen the burden on the secondary and tertiary care centers and provide better and broader access to insulin for many patients with diabetes. Better harmonization between the public and private healthcare sectors for insulin provision is required through better legalization of the insulin cost limits in both sectors.

The countries that are not insulin manufacturers, or where the production is not enough to fulfill the national need, had to secure their insulin share from multiple manufacturers with the best quality measures to decrease the insulin monopoly.

Developing the integrative well-funded long-term plan for R&D for diabetes care is necessary, along with building a collaborative network with the big insulin manufacturers to use it as a base to build the national insulin manufacturers with adequate national human resources. The Saudi and Algerian experiences with Novo Nordisk and Eli Lilly are clear examples of such collaboration. The R&D may include the insulin delivery system because innovation in the types of insulin might not be necessary.

The MENA countries must build or adopt country-specific solid specific quality standards to register the generic insulin into the country's healthcare, even if the insulin passes the insulin prequalification program by the WHO.

The big insulin manufacturers should apply a better differential pricing (like that for Afghanistan, Sudan, and Yemen) for other countries in the regions and consider the unique situation of countries in economic or humanitarian crises.

A comprehensive and culturally appropriate diabetes lifestyle education program for diabetics and their healthcare givers should be provided. The program should include training of the HCW on better diabetes care.

Healthcare authorities must provide complete or partial plans for insurance, procurement, and reimbursement according to the country-specific characteristics depending on the country's economy and population characteristics.

All MENA countries must develop a disaster preparedness plan and national diabetes care guidelines during the humanitarian crisis to mitigate the effect of disasters on their population. Ensure the continuation of the action of the humanitarian aid organizations for the diabetes care provision for vulnerable populations in remote areas where diabetes care is not accessible and hard to reach or for the population within conflict areas with suboptimal health conditions.

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Challenges

None.

Limitations

None.

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